

8EHQ-0902-15177



8EHQ-02-15177

September 5, 2002

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Attention: TSCA Section 8(e) Coordinator

Re: Pyrolysis C5 – OECD 422 Study in Rats by Inhalation Exposure -
Submission of Supplemental Information

Dear Madam or Sir:

On August 2, 2002, the American Chemistry Council Olefins Panel (Panel) submitted a letter on behalf of certain of its members (listed below) pursuant to Section 8(e) of the Toxic Substances Control Act (TSCA) to inform EPA of preliminary histopathology results from a OECD 422 study that was conducted for Pyrolysis C5 in rats. The Panel now has some additional histopathology information from the same study and is submitting it as a supplement to the August 2, 2002 submission.

Pyrolysis C5 was tested pursuant to the Olefins Panel's testing plan for the C5 non-Cyclics Category under the High Production Volume Chemical Challenge Program.¹ The Pyrolysis C5 stream is a hydrocarbon distillate fraction separated from pyrolysis gasoline. The Pyrolysis C5 stream consists primarily of C5 dienes and other C5 hydrocarbons and low levels of higher boiling C4 hydrocarbons and volatile C6 hydrocarbons. CAS Registry numbers that are used by Panel members to identify pyrolysis C5 streams include: 68476-55-1 (Hydrocarbons, C5-rich), 68476-43-7 (Hydrocarbons, C4-6, C5 rich), 68527-19-5 (Hydrocarbon, C1-4, debutanizer fraction), 68603-00-9 (Distillates, petroleum, thermal cracked naphtha and gas oil) and 68956-55-8 (Hydrocarbons, C5-unsaturated).

Initially, histopathology was conducted on tissues from high dose and control animals only; preliminary results from that review were reported in the August 2 submission. Since there were some findings in the liver and kidney, the Panel subsequently conducted a

¹ The test plan is available at <http://www.epa.gov/chemrtk/olefins/olefintp.pdf>.



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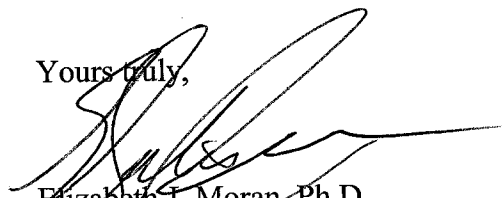
histopathology review of the liver and kidney tissues from animals treated at the two lower doses. As the attached histopathology report indicates, effects were not seen in the livers of the mid- and low dose males and females. Some effects were seen in the kidneys in the mid and low dose males, but not females.

A final report is not available at this time but will be forwarded when received from the laboratory.

The following members of the Panel produce one or more of the streams included in the C5 non-Cyclics Category and are sponsors of the testing for the category: BP Amoco Chemical Company, Chevron Phillips Chemical Company LP, The Dow Chemical Company, Equistar Chemicals, LP, ExxonMobil Chemical Company, The Goodyear Tire & Rubber Company, Huntsman Corporation, NOVA Chemicals Inc., and Shell Chemical Company LP.

If you have any questions, please contact me at 301 924 2006 or at Elizabeth_Moran@americanchemistry.com.

Yours truly,



Elizabeth J. Moran, Ph.D.
Manager, Olefins Panel

Attachments

cc: Richard H. Hefter (MC 7403)

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HISTOPATHOLOGY REPORT

Treatment-related changes

Liver

Centrilobular hepatocyte hypertrophy, minimal in degree was detected in High dose males and females. This finding was not seen in rats from the lower dosage groups or controls. This finding correlates with the slightly higher bodyweight adjusted liver weights seen in High dose male and female rats.

Group		Male				Female			
		Control	Low	Inter	High	Control	Low	Inter	High
Hepatocyte hypertrophy – Centrilobular	Minimal	0	0	0	8	0	0	0	4
	Total	0	0	0	8b	0	0	0	4
Number examined		12	12	12	12	12	12	12	12

b - $p < 0.01$, with Fisher's Exact Test, on Totals only

Kidneys

Cortical tubules with hyaline droplets, minimal to marked in degree, related in severity to increasing dose, were detected in all treated groups of male rats. This finding correlates with the increased adjusted group mean kidney weights seen in all treated groups of males.

An increased degree of cortical tubular basophilia was detected in all treated groups of male rats. A marginal increases in basophilic/dilated cortical tubules, cortical scarring and medullary tubular basophilia was also detected in High dose male rats. A marginal increase in medullary tubular basophilia was also detected in Inter Group male rats

No similar findings were seen in female rats to account for the increased kidney weight seen in High dose females. A focus of basophilic/dilated cortical tubules was seen in the kidneys of two High dose and one Low dose female rat. This minor finding on its own was not considered to be of toxicological importance.

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Group		Control	Male			Control	Female		
			Low	Inter	High		Low	Inter	High
Cortical tubules with hyaline droplets									
	Minimal	0	7	0	0	0	0	0	0
	Slight	0	5	2	0	0	0	0	0
	Moderate	0	0	10	4	0	0	0	0
	Marked	0	0	0	8	0	0	0	0
	Total	0	12c	12c	12c	0	0	0	0
Cortical tubular basophilia									
	Minimal	11	8	8	8	3	7	4	3
	Slight	0	3	4	4	0	0	0	0
	Total	11	11	12	12	3	7	4	3
Basophilic/dilated cortical tubules									
	Minimal	0	1	0	3	0	1	0	2
	Total	0	1	0	3	0	1	0	2
Cortical scarring									
	Minimal	2	1	2	4	0	1	0	0
	Total	2	1	2	4	0	1	0	0
Medullary tubular basophilia									
	Minimal	0	0	2	2	0	0	0	0
		0	0	2	2	0	0	0	0
Number examined		12	12	12	12	12	12	12	12

c- $p < 0.001$, with Fisher's Exact Test, on Totals only

Incidental findings

All other microscopic findings recorded were considered to be incidental and of no toxicological importance.

Conclusion

Centrilobular hepatocyte hypertrophy was seen in the liver of High dose male and female rats.

In the kidney, cortical tubules with hyaline droplets and an increased degree of cortical tubular basophilia were seen in male rats from all treated groups. Associated with these changes were marginal increases in cortical scarring, basophilic/dilated cortical tubules and medullary tubular basophilia in High dose males and a marginal increase in medullary tubular basophilia in the Inter dose males.

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August 2, 2002

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Attention: TSCA Section 8(e) Coordinator

Re: Pyrolysis C5 – OECD 422 Study in Rats by Inhalation Exposure

Dear Madam or Sir:

The American Chemistry Council Olefins Panel submits this letter on behalf of certain of its members (listed below) pursuant to Section 8(e) of the Toxic Substances Control Act (TSCA) to inform EPA of preliminary histopathology results from a OECD 422 study that was conducted for Pyrolysis C5 in rats. The Panel has not made a determination as to whether a significant risk of injury to health or the environment is actually presented by the preliminary findings.

Pyrolysis C5 was tested pursuant to the Olefins Panel's testing plan for the C5 non-Cyclics Category under the High Production Volume Chemical Challenge Program.¹ The Pyrolysis C5 stream is a hydrocarbon distillate fraction separated from pyrolysis gasoline that consists primarily of C5 dienes and other C5 hydrocarbons and low levels of higher boiling C4 hydrocarbons and volatile C6 hydrocarbons. CAS Registry numbers that are used by Panel members to identify pyrolysis C5 streams include: 68476-55-1 (Hydrocarbons, C5-rich), 68476-43-7 (Hydrocarbons, C4-6, C5 rich, 68527-19-5 (Hydrocarbon, C1-4, debutanizer fraction), 68603-00-9 (Distillates, petroleum, thermal cracked naphtha and gas oil) and 68956-55-8 (Hydrocarbons, C5-unsatd.).

¹ The test plan is available at <http://www.epa.gov/chemrtk/olefins/olefintp.pdf>.

The preliminary histopathology results of the 422 study were reported in a laboratory study update memorandum (attached) that described the findings for all (12/sex/group) control and high dose (1000 ppm) animals and a few low (100 ppm) and mid dose (300 ppm) animals that exhibited gross lesions at necropsy. A summary of the histopathology results follow:

Liver

Centrilobular hepatocyte hypertrophy, minimal in degree, was detected in 8 and 4 high dose males and females, respectively. This finding correlates with the slightly higher bodyweight adjusted liver weights seen in high dose male and female rats.

Kidneys

Cortical tubules with hyaline droplets, moderate to marked in degree, were detected in all male high dose rats. This finding correlates with the increased adjusted group mean kidney weights seen in high dose males. These changes were not observed in the high dose females or control groups.

An increased degree of cortical tubular basophilia was detected in male rats. Marginal increases in basophilic/dilated cortical tubules was detected in 3 high dose male rats. Cortical scarring (minimal) and medullary tubular basophilia was detected in 4 and 2 high dose male rats, respectively.

No similar findings were seen in female rats to account for the increased kidney weight seen in high dose females. A minor finding of a focus of basophilic/dilated cortical tubules was seen in the kidneys of two high dose females.

A final report is not available at this time but will be forwarded when received from the laboratory.

Letters were submitted earlier this year by three Panel members pursuant to Section 8(e) of TSCA, describing preliminary results from the dose range finding study that was conducted for this OECD 422 study. These letters were submitted by Equistar Chemicals, LP on April 26, 2002 (8EHQ-02-15137), The Dow Chemical Company on May 2, 2002 (8EH number not available) and Chevron Phillips Chemical Company on May 3, 2002 (8EHQ number not available).

The following members of the Panel produce one or more of the streams included in the C5 non-Cyclics Category and are sponsors of the testing for the category: BP Amoco Chemical Company, Chevron Phillips Chemical Company LP, The Dow Chemical Company, Equistar Chemicals, LP, ExxonMobil Chemical Company, The Goodyear Tire & Rubber Company, Huntsman Corporation, NOVA Chemicals Inc., and Shell Chemical Company LP.

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August 2, 2002

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If you have any questions, please call Elizabeth Moran, Manager of the Olefins Panel, at 301 924 2006, write her at the address given at the bottom of the first page of this letter, or e-mail her at Elizabeth_Moran@americanchemistry.com.

Sincerely yours,

Courtney M. Price
Vice President, CHEMSTAR

cc: Richard H. Hefter (MC 7403)

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PRELIMINARY HISTOPATHOLOGY REPORT

Treatment-related changes

Liver

Centrilobular hepatocyte hypertrophy, minimal in degree was detected in High dose males and females. This finding correlates with the slightly higher bodyweight adjusted liver weights seen in High dose male and female rats.

Group		Male				Female			
		Control	Low	Inter	High	Control	Low	Inter	High
Hepatocyte hypertrophy –									
Centrilobular	Minimal	0	-	-	8	0	-	-	4
	Total	0	-	-	8	0	-	-	4
Number examined		12	0	0	12	12	0	0	12

Kidneys

Cortical tubules with hyaline droplets, moderate to marked in degree were detected in all male High dose rats. This finding correlates with the increased adjusted group mean kidney weights seen in High dose Males.

An increased degree of cortical tubular basophilia with marginal increases in basophilic/dilated cortical tubules, cortical scarring and medullary tubular basophilia was detected in High dose male rats.

No similar findings were seen in female rats to account for the increased kidney weight seen in High dose females. A focus of basophilic/dilated cortical tubules was seen in the kidneys of two High dose females. This minor finding on its own was not considered to be of toxicological importance.

Group		Male				Female			
		Control	Low	Inter	High	Control	Low	Inter	High
Cortical tubules with hyaline droplets									
	Minimal	0	2	0	0	0	0	-	0
	Slight	0	1	0	0	0	0	-	0
	Moderate	0	0	4	4	0	0	-	0
	Marked	0	0	0	8	0	0	-	0
	Total	0	3	4	12	0	0	-	0
Cortical tubular basophilia									
	Minimal	11	1	1	8	3	1	-	3
	Slight	0	1	3	4	0	0	-	0
	Total	11	2	4	12	3	1	-	3
Basophilic/dilated cortical tubules									
	Minimal	0	0	0	3	0	0	-	2
	Total	0	0	0	3	0	0	-	2
Cortical scarring									
	Minimal	2	1	2	4	0	0	-	0
		2	1	2	4	0	0	-	0
Medullary tubular basophilia									
	Minimal	0	0	0	2	0	0	-	0
		0	0	0	2	0	0	-	0
Number examined		12	3	4	12	12	1	0	12

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